influenza A viruses isolated in Kenya in 2008-2009 despite lack of widespread antiviral use.

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Fluoroquinolone resistance via *qnrA* integron cassette in ESBL producing *Escherichia coli* clinical isolates from Thailand

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Background: Although *qnrA*, encoding quinolone resistance protein, confers low-level resistance to fluoroquinolone, its role in quinolone resistance when associated with other resistant mechanisms remains unknown.

Methods: One hundred extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* were collected from Siriraj Hospital (Bangkok, Thailand) and tested for *qnrA* by PCR. All *qnrA* positive isolates were investigated for *gyrA* mutations and a presence of class 1 integron by DNA sequencing and PCR. The locations of *qnrA* and *intI1* genes were analyzed by Southern blot hybridization. Phenotypic characteristics were studied by antimicrobial susceptibility test and time kill method.

Results: *qnrA* genes were found in 8% of ESBL-positive *E. coli* (8/100), confirmed to be *qnrA1* by DNA sequencing. All *qnrA1* positive isolates also harbored *intI1* gene. Double mutations (S83L and D87N) in *gyrA* were found in 50% (4/8) of *qnrA1* positive isolates. Specific *qnrA1* and *intI1* probes showed both *qnrA1* and *intI1* genes could be found on the chromosome and/or plasmids. Some isolates possessed two integron elements. The MIC (ciprofloxacin) against the isolate harboring both *qnrA1* and *gyrA* with double mutations was 2-fold higher than that against the isolate with only *gyrA*, and was much higher than that against the isolate harboring only *qnrA1* (MICs of 64 μg/ml, 32 μg/ml, and 0.12 μg/ml, respectively). According to the time kill study, 0.5 μg/ml of ciprofloxacin showed bactericidal activity after six hours of incubation against the isolate harboring only *qnrA1*. The bacteriostatic activity against the isolate harboring only *gyrA* with double mutations could be observed when the concentrations of ciprofloxacin were ≤256 μg/ml. The regrowth of the isolate carried both genes in 64-128 μg/ml at 24 hours of incubation were observed. Only 512 μg/ml of ciprofloxacin showed bactericidal activity after four hours of incubation against the isolate harboring both *qnrA1* and *gyrA* with double mutations.

Conclusion: *qnrA* could integrate into the chromosome by class 1 integrons. Presence of fluoroquinolone resistance elements on both plasmid and chromosome indicated high selection pressure in *E. coli* and, may be, in other Gram-negative bacteria as well. The *qnrA* gene conferred higher-level ciprofloxacin resistance on double mutations in *gyrA* (S83L and D87N) background.

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Trends in antimicrobial susceptibility among bacterial isolates from respiratory tract infections in Japanese hospitals participating in the Levofloxacin Surveillance Group during the period 1994-2010

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Background: Fluoroquinolones (FQs) are among the most commonly antimicrobials used to treat respiratory tract infections (RTI). FQ resistance is still very rare for *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Moraxella catarrhalis* and *Haemophilus influenzae*. However, FQ resistance in these organisms has been sporadically reported over the past several years. We have already performed nationwide surveillance on resistance for FQ and other antimicrobials in many bacterial clinical isolates in Japan since 1994. We report herein surveillance data from 1994 to 2010 for the aforementioned causative pathogens of RTI.

Methods: A total of 14,179 clinical isolates of the 4 species were collected from 92 centers participating in the Levofloxacin Surveillance Group from 1994 to 2010 in Japan, and susceptibility to 17 antibiotics was tested by broth microdilution methods according to the Clinical Laboratory Standards Institute (CLSI) guidelines. Quinolone resistance-determining region (QRDR) mutations in gyrA, gyrB, parC, or parE were also identified by direct sequencing method.

Results: 1. *S. pneumoniae*: The resistance rate for levofloxacin has fluctuated at a low level of 1.06±0.71% (geometric mean±SD). Interestingly, the peak value of MIC distribution in levofloxacin-susceptible isolates shifted from 0.5 μg/mL to 1.0 μg/mL from 2004 to 2007. QRDR-mutations were found in some of the LVFX-susceptible isolates. The susceptibility to macrolides also declined over time.

2. *S. pyogenes*: A high level of susceptibility to FQs, cephalosporins, carbapenems was maintained, but the susceptibility to macrolides has rapidly decreased since 2002.

3. *M. catarrhalis*: *M. catarrhalis* maintained a susceptible rate of almost 100% for FQs, the advanced-generation cephalosporins, carbapenems and macrolides.

4. *H. influenzae*: Resistant isolates for levofloxacin were not found or were very few if any. The rate of β-lactamase-negative ampicillin-resistant has rapidly increased from 25.8% in 2002 to 57.9% in 2010.

Conclusion: Levofloxacin still maintained a high level of antimicrobial activity against *S. pneumoniae*, *S. pyogenes*, *M. catarrhalis* and *H. influenzae*, and remains a useful therapeutic drug for RTI.

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